

### **REMARKS**

This submission is in response to the rejection issued by the USPTO on October 16, 2008. Claims 1 - 8 and 11 - 19 have been cancelled. Claim 9 has been amended. A typographical error was corrected. The concentration of ethanol was revised to 40 v/v% from 35 v/v%. Support for this limitation, in admixture with the other components of claim 9 may be found on page 22, line 20; page 31, line 9; page 32 in Table 2 and at line 18 on page 32.. Additionally the use listed in the preamble has been removed. New claims 20-22 have been added and are discussed in greater detail below.

### **Correction to Priority Claim**

The USPTO has stated that this application is only entitled to an effective filing of January 22, 2004. This is incorrect and the undersigned respectfully requests that the USPTO correct its records.

Attached to this submission as Exhibit A is a copy of a preliminary amendment submitted on behalf of the Applicant, claiming priority to a U.S provisional application filed on February 3, 2003 (U.S. Serial number 60/444,496). The preliminary amendment was submitted on July 29, 2005 when Applicants entered the national phase. The USPTO's date stamp, (in the top right hand corner of the document) documents that the USPTO received this priority claim in a timely manner (i.e. in compliance with the 4 month deadline specified 37 CFR 1.78 (a) (2) and (a) (5)). The undersigned requests the USPTO to correct the priority claim as shown above.

### **Rejections Under 35 USC 101 and 112**

Claims 11 - 19 were rejected under 35 USC 101 and claims 2 - 8 were rejected under 35 USC 112. The cancellation of these claims renders this rejection moot.

### **Rejection Under 35 USC 103**

Remaining claim 9 is rejected under 35 USC 103 over Biedermann, et al (hereinafter Biedermann) in view of Hu. The USPTO asserts that Biedermann discloses topical compositions that contain water, propylene glycol or ethanol. Further, these compositions may optionally contain dimethyl isorbide or hexylene glycol. The USPTO further asserts it would be obvious to incorporate the 4-cyclopentyl resorcinol of Hu into

the formulation of Biedermann. It is respectfully submitted this rejection is in error and should be withdrawn.

Biedermann discloses topical compositions for alleviating oily skin. The active is niacinamide. Biedermann discloses this composition should be incorporated into a "cosmetically acceptable carrier". Such a carrier is suitable for contact with human skin. Biedermann discloses numerous excipients that may be applied to the skin, beginning at column 5 and continuing thru column 10. Biedermann does not indicate any particular preference for any excipient.

Hu does disclose 4-cyclopentyl resorcinol and its use as a depigmentation agent. More specifically, in Example 7, it discloses a formulation containing this compound in admixture with ethanol and propylene glycol, in a 70/30 ratio (v/v).

Nothing in Biedermann would lead one of ordinary skill in the art to expect that the pharmacological activity of the active could be enhanced by the particular choice of carrier. The USPTO's rejection implicitly states that the composition of Hu and claim 9 should have the same relative efficacy in animal models of depigmentation. Further, any such difference would be unexpected and would objective evidence of non-obviousness.

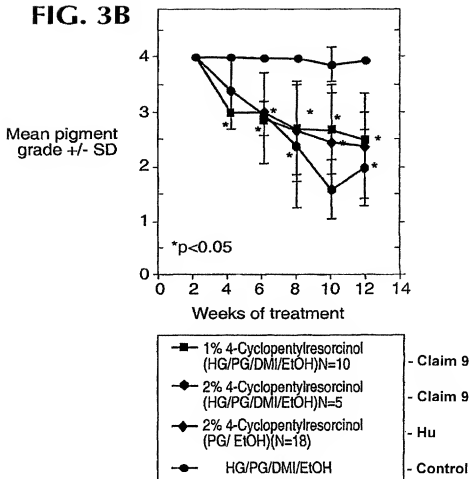
The USPTO's attention is also directed to Example 1, beginning on page 28 of Applicant's specification. This example summarizes a number of experiments in which the depigmenting activity of 4-cyclopentyl resorcinol was evaluated in alternative formulations in an in-vivo animal model, including the formulation of Hu described above.

This animal model used Yucatan swine. These pigs have dark skin. This allows researchers to visually observe changes in pigmentation and to grade the change using a predetermined scoring system. A lower number reflects less pigmentation and thus, a **greater** depigmenting effect by a given formulation.

These test formulations were applied to the pigs back twice daily; 5 days per week; for up to 12 weeks and the changes in pigmentation were evaluated by 3 times per week using the standardized scoring described on page 29.

One of the test groups directly compared the formulation of Hu with that of claim 9. The formulation that was representative of Hu was a solution of ethanol/propylene glycol (70/30) containing 2% 4-cyclopentyl resorcinol. This was compared against the composition of claim 9 containing both 1% and 2% 4-cyclopentyl resorcinol. The results are depicted graphically in Figure 3B and are reproduced below for the USPTO's convenience.

**FIG. 3B**



A visual review of the data shown in this slide demonstrates the unexpected superiority of the formulation of claim 9. The formulation of claim 9, containing only 1 w/v% of 4-cyclopentyl resorcinol demonstrated essentially the same depigmenting effects as the formulation of Hu that contained twice the concentration of active (i.e. 2 w/v %). At the conclusion of the 12 week testing period, both formulations showed a mean pigmentation score of approximately 2.5 (despite the differing concentrations of 4-cyclopentyl resorcinol).

The formulation of claim 9 that contained the same quantity of active as Hu (i.e. 2 w/v %) was clearly superior. At the conclusion of the 12 week testing period, the

formulation of claim 9 had a mean pigmentation score of approximately 2 versus 2.5 for Hu.

Nothing in Biedermann would have suggested this result. Biedermann merely discloses a substantial list of excipients that are safe for topical application to humans. Nothing in Biedermann would suggest that any of these excipients could impact the relative efficacy of 4-cyclopentyl resorcinol, let alone those specifically required by claim 9. The secondary reference Hu does not cure this deficiency.

As the USPTO has outlined in its latest communication, any inquiry regarding obviousness needs to include a consideration of unexpected results. The data above shows such unexpected results. Applicant's choice of specific excipients has allowed them to reduce the required dosage of 4-cyclopentyl resorcinol by up to 50%. Such data clearly shows the unobviousness of claim 9.


New claim 20 provides a dosage range for the 4-cyclopentyl resorcinol. New claim 21 is closed, having the transitional phrase "consisting of" further defining over the prior art.

Withdrawal of the rejections of record and reconsideration is respectfully requested.

Date: 3/6/09

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Respectfully submitted,

  
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appl. No. : TBD  
Applicant : NARI, XINA  
Filed : TBD  
Title : IMPROVED FORMULATION FOR SKIN-LIGHTING AGENTS  
TC/AU : TBD  
Examiner : TBD  
Docket No. : PC23207A  
Customer No. : 28880

Commissioner for Patents  
PO Box 1450  
Alexandria, VA 22313-1450

**Preliminary Amendment Under 37 CFR 1.115**

Sir:

Prior to calculating the filing fee, please enter the following preliminary amendment.

Amendments to the Specification begin on page 2 of this paper.

Amendments to the Claims are reflected in the listing of claims which begin on page 3 of this paper.

Remarks begin on page 6 of this paper.

**Amendments to the Specification:**

Please insert the following Cross Reference to Related Application section as the first paragraph in the specification, immediately following the title:

**CROSS REFERENCE TO RELATED APPLICATION**

This U.S. Utility application claims priority from PCT/IB2004/000240, filed January 22, 2004, which claims priority from United States provisional application number 60/444,496 filed on February 3, 2003.

REMARKS

The claim to priority has been updated. Authorization to charge the fee and any additional fees as necessary or credit overpayment to deposit account 23-0455 is hereby given.

Date: 7/29/05

Respectfully submitted,

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